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(54) Title: **RGD-ENRICHED GELATINE-LIKE PROTEINS WITH ENHANCED CELL BINDING**

(57) Abstract: The invention concerns a cell support comprising an RGD-enriched gelatine that has a more even distribution of RGD sequences than occurring in a natural gelatine and with a minimum level of RGD sequences. More precisely the percentage of RGD sequences related to the total number of amino acids is at least 0.4 and if the RGD-enriched gelatine comprises 350 amino acids or more, each stretch of 350 amino acids contains at least one RGD motif. Preferably the RGD-enriched gelatines are prepared by recombinant technology, and have a sequence that is derived from a human gelatine or collagen amino acid sequence. The invention also relates to RGD-enriched gelatines that are used for attachment to integrins. In particular the RGD-enriched gelatines of the invention are suitable for coating a cell culture support for growing anchor-dependent cell types. Further, the RGD-enriched gelatines of the invention may find use in medical applications, in particular as a coating on implant or transplant material or as a component of drug delivery systems.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL2004/000208

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/78 C12N5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 140 072 A (CAPPELLO JOSEPH ET AL) 31 October 2000 (2000-10-31) SEQ ID NO:66 column 36, line 1 - column 41, line 52	1-9,15
X	WO 98/18918 A (COMMW SCIENT IND RES O) 7 May 1998 (1998-05-07) page 4, line 35 - page 6, line 15 page 25, line 22 - line 30	1-9,15
A	WO 02/064625 A (ADP PHARMACEUTICA) 22 August 2002 (2002-08-22) SEQ ID NO:22 page 73, line 12 - line 22	1-11,14, 15
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

21 September 2004

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16. 02. 2005

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INTERNATIONAL SEARCH REPORT

Intern Application No
PCT/NL2004/000208

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WIERZBA A ET AL.: "PRODUCTION AND PROPERTIES OF A BIFUNCTIONAL FUSION PROTEIN THAT MEDIATES ATTACHMENT OF VERO CELLS TO CELLULOSIC MATRICES" BIOTECHNOLOGY AND BIOENGINEERING. INCLUDING: SYMPOSIUM BIOTECHNOLOGY IN ENERGY PRODUCTION AND CONSERVATION, JOHN WILEY & SONS. NEW YORK, US, vol. 47, 20 July 1995 (1995-07-20), pages 147-154, XP002023829 ISSN: 0006-3592 the whole document</p> <p>-----</p>	1-11, 14, 15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NL2004/000208

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11, 14, 15 completely

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11,14,15 (completely)

A cell support comprising RGD-enriched gelatine, whereby said gelatine contains at least 0.4% RGD motifs and if said gelatine comprises 350 amino acids or more, each stretch of 350 amino acids contains at least one RGD motif.

2. claims: 12,13 (completely)

An RGD-enriched gelatine, whereby said gelatine contains at least 0.4% RGD motifs and if said gelatine comprises 350 amino acids or more, each stretch of 350 amino acids contains at least one RGD motif and said gelatine consists for at least 80% of one or more parts of native human collagen sequences and said parts of native human collagen sequences have a length of at least 30 amino acids.

3. claim: 16

Use of an RGD- enriched gelatine as a component of drug delivery systems.

4. claim: 17

Use of an RGD- enriched gelatine as a component for inhibition of cancer metastasis.

5. claim: 18

Use of an RGD- enriched gelatine as a component of prevention of platelet aggregation.

6. claim: 19

Use of an RGD- enriched gelatine as a component after surgery to prevent tissue adhesion.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/NL2004/000208

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